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Protective effect of curcumin and vitamin C each alone and in combination on cisplatin-induced sperm abnormalities in male albino rats

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Abstract Infertility is a major concern for young men of reproductive age under-going chemotherapy. Unfortunately, chemotherapeutic treatment for neoplastic diseases commonly impairs fertility either temporally or permanently. In general, chemotherapeutic agents in cancer treatments target all rapidly growing healthy cells, such as those of reproductive system in addition to tumor tissues and it therefore results in impairment of spermatogenesis leading to abnormalities in sperm morphology in cancer survivors. Consequently, antioxidants have been shown to protect nonmalignant cells and organs against damage by chemotherapeutic agents. Hence the present study was designed to evaluate the possible ameliorative role of curcumin or vitamin C alone and their combination in alleviating the toxicity of cisplatin on sperm morphology when given to normal albino rats.

The results of the present investigation concluded that the combination between curcumin and vitamin C in cisplatin treatment afforded the best ameliorative effect on cisplatin induced sperm shape abnormalities. This may be due to the synergistic effect between curcumin and vitamin C as both of them have antioxidant properties which in turn lead to repairing of sperm abnormalities.

Introduction

Cisplatin (cis-diamminedichloroplatinum-II, CIS), one of the most effective and widely prescribed anticancer drugs, is still used in the treatment of many types of solid tumors including testicular cancer (Ahmed et al., 2011). It has been proven highly effective in curing testicular cancer in combination with other drugs even at an advanced stage of the disease (Peckham et al., 1983). Cisplatin (CIS) kills cancer cells by forming covalent adducts with the cellular DNA molecules and thereby terminating the vital processes like replication and transcription and inducing apoptosis (Johnson et al., 1998). The cytotoxic action of the drug is often thought to be associated with its ability to bind DNA to form cisplatin-DNA adducts (Goldstein and Mayor, 1983).

Zahra et al. (2014) concluded that percentage of normally shaped sperm was decreased in mice administered cisplatin at a single dose. Also, cisplatin decreased sperm motility and

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increased anomalous spermatozoa in rats (Aldemir et al., 2014).

Cisplatin toxicity is occurred by increased generation of reactive oxygen species (ROS) and decreased formation of antioxidants (Chirino and Pedraza-Chaverri, 2009). The production of ROS depends on the dose of cisplatin and the duration of treatment (Brozovic et al., 2010).

Therefore, it has become essential to supplement with antioxidants to reduce the toxicity created by anti-cancer drugs (Mohamed et al., 2011).

Antioxidants such as vitamin C reduces many cisplatin-associated side effects. Additionally, numerous natural products of plant origin protect against drug-induced toxicity (Antunes et al., 2001).

Vitamin C or ascorbic acid (L, 3-ketothreohexuronic acid lactone) is a water soluble vitamin with antioxidant properties. Ascorbic acid is an active reducing agent involved in different biological effects (Henson et al., 1991).

The treatment with a mixture of ascorbic acid and cisplatin should be very useful to ameliorate cisplatin-induced toxicities including nephrotoxicity, hepatotoxicity and testes/sperms anomalies (Amenla and Surya, 2015).

Azu et al. (2011) concluded that herbal plant extracts with protective effects against cisplatin -induced reproductive toxicities are due to the presence of antioxidant agents.

Curcumin is a major yellow pigment in turmeric ground rhizome of *Curcuma longa* (commonly known as turmeric) which is used widely as a spice and coloring agent in many foods for example curry, mustard and potato chips as well as beautifying agents and medications (Joe et al., 2004).

Curcumin has been claimed to be a potential anti-inflammatory agent with phyto-nutrient and bio-protective properties (Aggarwal and Sung, 2009). It has also shown to alleviate various forms of male reproductive disorders in experimental animals and thus to enhance fertility (Khorsandi et al., 2013). Curcumin was shown to be a potent scavenger of a variety of reactive oxygen species (Goel et al., 2008). So, it has been shown to have strong antioxidant activity and decreases oxidative stress (Igbal et al., 2003).

Omur and Coyan (2016) demonstrated that curcumin, methionine and ellagic acid have protective effects on ram sperm parameters. In addition, Ehab et al. (2014) recorded that the treatment of rats with curcumin caused protective effect against cisplatin-induced testicular disorders. The sperm abnormality significantly decreased in curcumin treated groups compared with cisplatin treated groups.

Materials and methods

Animals

Forty five (45) adult male albino rats (*Rattus norvegicus*) were selected for the present study. Their weights ranged from 200 to 210 g each. The animals were housed in an air conditioned animal house facility at 25 °C, under a controlled 12 h light/-dark cycle. The rats were reared on a standard pellet diet and tap water *ad libitum*.

Test chemicals

Cisplatin was purchased from the local pharmacy shop in Egypt. The drug was dissolved in 0.9% normal saline and was injected intraperitoneally in a dose level of (0.4 mg/kg b. wt) according to the literature Pratibha et al. (2006).

VitacidC (Vitamin C) was purchased from the local pharmacy shop in Egypt. The vitamin was dissolved in distilled water and was given orally in a dose level of (100 mg/kg b. wt) according to literature Rana and Ahmed (2012).

Curcuma longa extract (Curcumin) was purchased from National Bio Lab (medical laboratory) 15El Nour St, Floor 1, Dokki, Giza Egypt. Curcumin was suspended in 0.05% gum acacia solution then it was given orally at dose level of (20 mg/kg b.wt) according to literature Xu et al. (2007).

Experimental design

The study was performed on 45 mature male rats (*Rattus norvegicus*), divided into 9 main groups; each group was consisted of 5 rats as following:

i. *Water control group:* Animals received distilled water orally daily for 60 successive days.
ii. *Saline control group:* Animals were injected intraperitoneally with physiological saline (0.9% sodium chloride) daily for 60 successive days.
iii. *Acacia control group:* Animals orally received 0.05% gum acacia solution daily for 60 successive days using metallic stomach tube.
iv. *Curcumin treated group:* Animals received curcumin orally at a dose of (20 mg/kg) suspended in 0.05% gum acacia solution daily for 60 successive days using metallic stomach tube.
v. *Vitamin C treated group:* Animals were orally administered vitamin C at a dose of (100 mg/kg) dissolved in distilled water daily for 60 successive days using metallic stomach tube.
vi. *Cisplatin treated group:* Animals were injected intraperitoneally with cisplatin at a dose of (0.4 mg/kg) dissolved in physiological saline daily for 60 successive days.
vii. *Cisplatin + curcumin treated group:* Animals received curcumin (20 mg/kg) orally and after 20 min animals were injected intraperitoneally with cisplatin at a dose of (0.4 mg/kg) dissolved in physiological saline daily for 60 successive days.
viii. *Cisplatin + vitamin C treated group:* Animals received vitamin C (100 mg/kg) orally and after 20 min animals were injected intraperitoneally with cisplatin at a dose of (0.4 mg/kg) dissolved in physiological saline daily for 60 successive days.
ix. *Cisplatin + curcumin + vitamin C treated group:* Animals received curcumin (20 mg/kg) as well as vitamin C (100 mg/kg) orally and after 20 min animals were injected intraperitoneally with cisplatin at a dose of (0.4 mg/kg) dissolved in physiological saline daily for 60 successive days.